

Serial No. 10/789,956
Docket No. SHE0081.00

AMENDMENTS

In the Claims:

Please amend claims 1-30 and add new claim 62 as indicated below. Currently amended claims are presented with markings to indicate the changes made, wherein a ~~strikethrough~~ is used to designate deletions and underlining is used to designate additions.

1. (Currently Amended) A conjugate composition comprising a plurality of conjugates, wherein at least about 82% of conjugates in the composition each has one to three one, two or three water-soluble polymers covalently attached to a Factor VIII moiety, and further wherein each water-soluble polymer has a nominal average molecular weight in the range of greater than 5,000 Daltons to ~~about~~ 150,000 Daltons.
2. (Currently Amended) The composition conjugate of claim 1, wherein the ~~each~~ water-soluble polymer in each conjugate is selected from the group consisting of a poly(alkylene oxide), poly(vinyl pyrrolidone), poly(vinyl alcohol), polyoxazoline, and poly(acryloylmorpholine).
3. (Currently Amended) The composition conjugate of claim 2, wherein each water-soluble polymer is a poly(alkylene oxide).
4. (Currently Amended) The composition conjugate of claim 3, wherein each poly(alkylene oxide) is a poly(ethylene glycol).
5. (Currently Amended) The composition conjugate of claim 4, wherein the poly(ethylene glycol) is terminally capped with an end-capping moiety selected from the group consisting hydroxy, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, alkynoxy, substituted alkynoxy, aryloxy and substituted aryloxy.
6. (Currently Amended) The composition conjugate of claim 4, wherein the poly(ethylene glycol) is terminally capped with methoxy.

Serial No. 10/789,956
Docket No. SHEQ081.00

7. (Currently Amended) The composition conjugate of claim 4, wherein the poly(ethylene glycol) is terminally capped with hydroxy.

8. (Currently Amended) The composition conjugate of claim 4, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 6,000 Daltons to about 100,000 Daltons.

9. (Currently Amended) The composition conjugate of claim 8, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 10,000 Daltons to about 85,000 Daltons.

10. (Currently Amended) The composition conjugate of claim 9, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 20,000 Daltons to about 85,000 Daltons.

11. (Currently Amended) The composition conjugate of claim 10, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 53,000 Daltons to about 75,000 Daltons.

12. (Currently Amended) The composition conjugate of claim 3, wherein each water-soluble polymer is linear.

13. (Currently Amended) The composition conjugate of claim 3, wherein each water-soluble polymer is branched.

14. (Currently Amended) The composition conjugate of claim 3, wherein the Factor VIII moiety is selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF, and B-domain deleted Factor VIII, and deletion variants, substitution variants or addition variants of any of the foregoing.

Serial No. 10/789,956
Docket No. SHE0081.00

15. (Currently Amended) The composition conjugate of claim 14, wherein the Factor VIII moiety is selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, and Factor VIII:vWF.

16. (Currently Amended) The composition conjugate of claim 14, wherein the Factor VIII moiety is B-domain deleted Factor VIII.

17. (Currently Amended) The composition conjugate of claim 3, wherein the Factor VIII moiety is recombinantly derived.

18. (Currently Amended) The composition conjugate of claim 3, wherein the Factor VIII moiety is blood-derived.

19. (Currently Amended) The composition of claim 3 62, wherein the composition is substantially free of albumin.

20. (Currently Amended) The composition of claim 3 62, wherein the composition is substantially free of proteins that do not have Factor VIII activity.

21. (Currently Amended) The composition of claim 3 62, wherein the composition is substantially free of noncovalently attached water-soluble polymers.

22. (Currently Amended) The composition of claim 3 62, wherein at least one water-soluble polymer is covalently attached to a site in the active form of the moiety having Factor VIII activity.

23. (Currently Amended) The composition of claim 1 62, in lyophilized form.

24. (Currently Amended) The composition of claim 1 62, in the form of a liquid.

Serial No. 10/789,956
Docket No. SHE0081.00

25. (Currently Amended) The composition of claim 4 62, further comprising a pharmaceutically acceptable excipient.

26. (Currently Amended) The composition conjugate of claim 1, wherein each conjugate comprises an amide linkage.

27. (Currently Amended) The composition conjugate of claim 1, wherein each conjugate comprises a secondary amine linkage.

28. (Currently Amended) The composition conjugate of claim 1, wherein each conjugate comprises a carbamate linkage.

29. (Currently Amended) The composition conjugate of claim 1, wherein each conjugate comprises a thioether linkage.

30. (Currently Amended) The composition conjugate of claim 1, wherein each conjugate comprises a disulfide linkage.

31. (Withdrawn) A composition comprising a plurality of monoPEGylated Factor VIII moiety conjugates.

32. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises one poly(ethylene glycol) terminally capped with an end-capping moiety selected from the group consisting hydroxy, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, alkynoxy, substituted alkynoxy, aryloxy and substituted aryloxy.

33. (Withdrawn) The composition of claim 31, wherein the poly(ethylene glycol) is terminally capped with methoxy.

34. (Withdrawn) The composition of claim 31, wherein the poly(ethylene glycol) is terminally capped with hydroxy.

Serial No. 10/789,956
Docket No. SHE0081.00

35. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a poly(ethylene glycol) having a nominal average molecular weight in the range of greater than 5,000 Daltons to about 150,000 Daltons.

36. (Withdrawn) The composition of claim 35, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 6,000 Daltons to about 100,000 Daltons.

37. (Withdrawn) The composition of claim 36, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 10,000 Daltons to about 85,000 Daltons.

38. (Withdrawn) The composition of claim 37, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 20,000 Daltons to about 85,000 Daltons.

39. (Withdrawn) The composition of claim 38, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 53,000 Daltons to about 75,000 Daltons.

40. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a linear poly(ethylene glycol).

41. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety comprises a branched poly(ethylene glycol).

42. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a Factor VIII moiety selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF, B-domain deleted Factor VIII, and

Serial No. 10/789,956
Docket No. SHE0081.00

biologically active fragments, deletion variants, substitution variants or addition variants of any of the foregoing.

43. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a Factor VIII moiety selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, and Factor VIII:vWF.

44. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises B-domain deleted Factor VIII.

45. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a Factor VIII moiety that is recombinantly derived,

46. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a Factor VIII moiety that is blood-derived.

47. (Withdrawn) The composition of claim 31, wherein the composition is substantially free of albumin.

48. (Withdrawn) The composition of claim 31, wherein the composition is substantially free of proteins that do not have Factor VIII activity.

49. (Withdrawn) The composition of claim 31, wherein the composition is substantially free of noncovalently attached water-soluble polymers.

50. (Withdrawn) The composition of claim 31, in lyophilized form.

51. (Withdrawn) The composition of claim 31, in the form of a liquid.

52. (Withdrawn) The composition of claim 31, further comprising a pharmaceutically acceptable excipient.

Serial No. 10/789,956
Docket No. SHE0081.00

53. (Withdrawn) The composition of claim 31, wherein each conjugate comprises an amide linkage.

54. (Withdrawn) The composition of claim 31, wherein each conjugate comprises a secondary amine linkage.

55. (Withdrawn) The composition of claim 31, wherein each conjugate comprises a carbamate linkage.

56. (Withdrawn) The composition of claim 31, wherein each conjugate comprises a thioether linkage.

57. (Withdrawn) The composition of claim 31, wherein each conjugate comprises a disulfide linkage.

58. (Withdrawn) A method for making a conjugate comprising contacting, under conjugation conditions, a Factor VIII moiety with a polymeric reagent.

59. (Withdrawn) A method for treating a patient in need of Factor VIII therapy, comprising the step of administering to the patient the composition of claim 1 or claim 31, wherein the composition contains a therapeutically effective amount the conjugates.

60. (Withdrawn) The method of claim 59, wherein the patient is suffering from hemophilia A.

61. (Withdrawn) The method of claim 59, wherein the patient is administered the composition within two days prior to undergoing surgery.

62. (New) A composition comprising the conjugate of claim 3.